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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/698,893	10/27/2000	Morey Kraus	07588-008001	5973

26161 7590 12/18/2002

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/698,893	KRAUS ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *12,22-24,28,42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-21,25-27 and 29-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 and 7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The preliminary amendment filed March 26, 2001 (Paper No. 2) has been entered. Claim 26 has been amended.

The preliminary amendment filed September 16, 2002 (Paper No. 8) has been entered. Claims 1 and 2 have been amended. Claims 42 and 43 have been newly added.

The response filed September 16, 2002 (Paper No. 8) has been entered. Applicants' election with traverse of Group IX, Claims 1-11, 13-21, 25-27, and 29-41, in Paper No. 8 is acknowledged. The elected invention is drawn to a method of treating stroke. The traversal is on the grounds that, because Groups I-IX are all classified in class 424, subclass 93.1, searching all groups poses no more burden than searching a single group, because in either case only a single class and subclass must be searched. However, this is not the case because the search is never limited to a search of the U.S. Patents Database. Other databases covering non-patent literature, foreign patent applications, and international patent applications must also be searched. Thus, a search for the method of the invention of Group IX would not identify art relevant to Groups I-VIII. Therefore, additional searching would be required to cover the inventions of Groups I-VIII. Because the searches are not coextensive, a search and examination of all 9 patentably distinct inventions in a single patent application would constitute a serious burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-42 are pending in the instant application.

Claims 12, 22-24, 28, 42, and 43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction requirement in Paper No. 8.

Accordingly, Claims 1-11, 13-21, 25-27, and 29-41 are examined herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 13-21, 25-27, and 29-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of causing improvement in function of the central nervous system in a mammal having a brain ischemia resulting from stroke, comprising injecting CD34+/-, Lin- cells into an ischemic region of the mammal's brain, does not reasonably provide enablement for the various methods of treating covered by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method of causing an improvement in function of the central nervous system of a subject having impaired central nervous system function by administering "cells derived from umbilical cord blood" or "cells derived from blood."

The specification discloses an example at pages 10-13 where male Sprague Dawley rats were subjected to an MCA occlusion and subsequently received an injection of CD34+/-, Lin- stem cells directly into the ischemic region of the brain. Some modest improvement was observed in two of the behavioral tests that the animals were subjected to following treatment: specifically, the forelimb placing test and the hindlimb placing test. No improvement was observed in 3 other behavioral tests that the animals were subjected to (i.e., swinging, cylinder, or paw reaching tests).

Thus, the working example is limited to transplantation of a specific cell type (CD34+/-, Lin-) isolated from a sample of fresh cord blood, into a rat that serves as a stroke model.

The state of the art is such that very little is known about the cell types that can be used to restore neurological function. One of the lingering questions in the field of stem cell research relates to the stage of differentiation of stem cells useful for transplantation and whether the same stage will be useful for all transplantation applications, or vary on a case-by-case basis (see p. ES-8, column 1 of Stem Cells: Scientific Progress and Future Research Directions, June 2001).

In a review of the state of the art of stem cell technology, the National Institutes of Health acknowledge the potential usefulness of stem cells in therapeutic transplantation and the possible development of therapeutic protocols in the future (see Stem Cells: Scientific Progress and Future Research Directions, June 2001). However, the review also illustrates that there are numerous and significant obstacles that must be overcome. As such, the asserted utility of the present invention, directed to using the claimed methods in therapeutic transplantation to treat stroke constitutes a credible utility, albeit one that is not enabled by the instant specification. The instant rejection therefore is not for lack of utility, but rather for lack of enablement for the asserted utility. For the reasons discussed herein, the specification does not teach how to use the claimed methods to produce a therapeutic effect over the full scope of the claim, which covers transplantation of a variety of cell types, as well as combined administration of cells and growth factors.

The specification fails to provide an enabling disclosure for the method of cell-based therapy because methods of transplantation of stem cells, precursor cells, and neural tissue into the CNS are not routinely successful and the specification does not offer adequate guidance to overcome the unpredictability in the art to enable one skilled in the art to practice the claimed method over the full scope to derive a therapeutic benefit in a diseased animal. The specification teaches that the only use for the claimed method of transplantation is to produce a therapeutic effect, but the specification does not adequately teach how to use the full scope of the claimed methods to produce such an effect. Jackowski et al. (1995) details the limitations and unpredictability associated with transplantation of neural tissue.

At page 311, column 1, paragraph 2, the reference discusses barriers to successful transplantation of neural tissue, notably the presence of molecules that actively inhibit the regeneration of mammalian CNS axons.

The specification fails to provide an enabling disclosure for producing a therapeutic effect using the claimed methods of therapeutic transplantation beyond the scope of enablement indicated above because the specification does not provide **specific guidance** for transplanting other cell types or for the combined administration of various cells and growth factors. In unpredictable arts, it is the specification itself that must provide the novel teachings for carrying out the claimed methods therapeutically. The working example is limited to transplantation of a specific cell type (CD34+/-, Lin-) isolated from a sample of fresh cord blood, into a rat that serves as a stroke model. The specification contemplates that "cells of the invention" can be used to treat a wide variety of neurodegenerative diseases, including stroke, Huntington's disease, Parkinson's disease, Alzheimer's disease, ALS, multiple sclerosis , Tay-Sacks, and cerebral palsy (page 4, lines 8-9). However, the elected invention is limited to methods of treating stroke. Accordingly, the specification must teach how to practice the full scope of the claimed methods of transplantation to produce a therapeutic effect in a patient having suffered from a stroke. Beyond the scope of enablement indicated above, the specification fails to provide specific guidance relating to the amount of cells to inject, the site of injection, and extent of cellular persistence required to provide a therapeutic benefit for stroke.

The court has recognized that physiological activity is unpredictable. *In re Fisher*, 166 USPQ 18 (CCPA 1970). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. *In re Fisher*, 166 USPQ 18 (CCPA 1970).

It is not to be left up to the skilled artisan to figure out how to make the necessary starting materials and then to figure out how to use them to produce the biological effects as recited in the claims.

The courts held that the disclosure of an application shall inform those skilled in the art how to use applicant's claimed invention, not how to **find out** how to use it for themselves. *In re Gardner et al.* 166 USPQ 138 (CCPA 1970) For the broad scope of the claims, this specification only teaches what is intended to be done and how it is intended to work, but does not actually teach how to do that which is intended.

Given the limited working examples, the limited guidance provided in the specification, the broad scope of the claims with regard to the various cell types to be transplanted and the combinations of cells and growth factors to be administered, and the unpredictability for producing a therapeutic effect upon transplantation of stem cells or precursor cells, undue experimentation would have been required for one skilled in the art to practice the full scope of the claimed methods of transplantation to produce a therapeutic effect in a stroke patient.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13-21, 25-27, and 29-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11, 13-21, 25-27, and 29-41 are indefinite because the claims are directed to treating any disorder of the central nervous system, but the elected invention is limited to methods of treating stroke. Thus, the metes and bounds of the claims are not clearly set forth.

Claims 1-11, 13-21, 25-27, and 29-41 are indefinite in their recitation of "causing an improvement in function of the central nervous system" in the preamble of the claims because there is no step where said "improvement" is effected.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE BAKER
PATENT EXAMINER